REMARKS/ARGUMENTS

Claims 10-15 are pending.

Claims 10-11 have been amended.

Claims 1-9 have been cancelled.

Claims 14-15 have been added.

Support for the amendments is found in the claims and specification (e.g., page 19, lines 17-21; page 21, Table II; pages 25-26, Table III; page 28, Table V; page 30, line 1-3) as originally filed. No new matter is believed to have been added.

Applicants wish to thank the Examiner for the meeting on February 1, 2008. The subject of the meeting included the rejection under 35 U.S.C. 112, second paragraph, in view of the proposed amendments. The Examiner indicated that claims 10, 12, and 14 in the form shown in the amendment are probably allowable. Concerning claim 11, the Examiner pointed out that claims 11, 13, and 15 will be probably allowable if the terms "an active chemical molecule," "a subject", and "the CNS disease" are defined in claim 11.

Applicants amend the specification by introducing sequence identifiers into Tables I, VII, VIII, and IX and request that the objection to the specification be withdrawn.

Applicants respond to the objection of claims 10-11 by correcting the term "an active chemical molecule" and request that the objection be withdrawn.

Claims 10-13 are rejected under 35 U.S.C. 112, second paragraph.

The Examiner is of the opinion that claims 10-11 are indefinite because the amount of the administered conjugate is not claimed. Applicants traverse.

A patent application is usually submitted at an early stage of drug development while a specific dose for a treatment is determined during clinical trials. It is clear for a person skilled in the art, specialist in drug development, that an active dose in a subject will depend on a number of parameters that need to be determined during the preclinical and phase IIa trials (*see* "Guidance for industry Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers," USDHHS, FDA, CDER, July 2005, submitted with this paper). The skill in the art is high and one knows to consider age, race, sex, weight and other factors when determining the amount sufficient to treat the subject and drive an active substance across the BBB to the CNS (see claims 10-11).

Concerning claims 14-15, the specification describes a dose administered to an animal model (mice). For example, on page 19, lines 8-9 and 19-20, it is described that mice were injected with a dose of 2 mg/kg and 2.5 mg/kg (equivalent in doxorubicine) (also, see Tables III and V on pages 25 and 28). On page 30, lines 3-4, a dose of 2 mg/kg is also used for dalargine alon and vectorized dalargine.

The lowest dose administered to a subject is calculated based on "Guidance for Industry," while the highest dose is estimated based on a common practice by pharmaceutical companies. According to the FDA "Guidance for Industry," the body surface area is taken into account, wherein a human dose is calculated as "Animal dose x 0.8 = Human dose" (i.e., 2mg/kg x 0.8 = 1.6 mg/kg) based on a lower dose exemplified in mice (2 mg/kg) (*see* Table 1 on page 7 of the "Guidance for Industry").

The highest dose is estimated without taking into account the body surface area and is directly extrapolated from the animal model to humans, i.e., Animal dose = Human dose (i.e., 2.5 mg/kg).

Accordingly, the reasonable range for administering the claimed compound to a subject is between 0.16 to 2.5 mg/kg based on the described experiments in the animal model.

Applicants also amended claim 11 to clarify that the claimed active substance is driven across the BBB to the CNS.

Applicants request that the rejection be withdrawn.

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

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